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Formal Allylation and Enantioselective Cyclopropanation of Donor/Acceptor Rhodium(II) Azavinyl Carbenes

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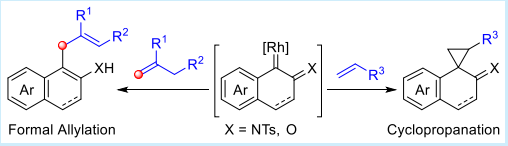
ABSTRACT: A highly efficient formal allylation of dihydronaphthotriazoles with alkenes under rhodium(II) catalysis is reported. Various allyl dihydronaphthalene derivatives were furnished via rhodium(II) azavinyl carbenes with moderate to good yields and excellent chemoselectivity. When monosubstituted alkenes are used, cyclopropanation occurs and good to excellent enantioselectivities have been achieved. Particularly noteworthy is the allylic C(sp^2)−H activation instead of traditional C(sp^3)−H activation in the formal allylation process.



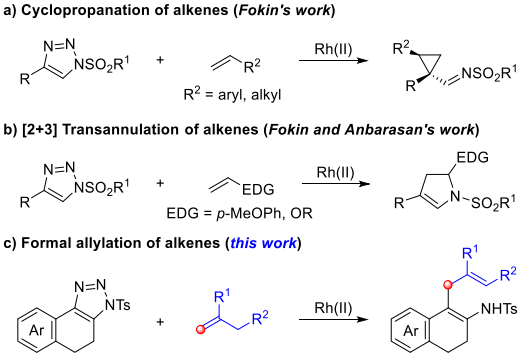
Donor/acceptor carbenes have emerged as significant reactive intermediates in related transformations,[1] such as C−H functionalization, cyclopropanation, etc. When the donor group attenuates the reactivity, donor/acceptor carbenes are more stable and often exhibit higher selectivity.[1g,h] However, the chemistry of donor/acceptor carbenes is limited by the potential safety issue of diazo compounds. Thus, developing alternative and stable carbene precursors is highly desired.

Recently, *N*-sulfonyl-1,2,3-triazole has become a hot topic in chemistry due to their role as a source of donor/acceptor carbene intermediates and versatile reactivity in the synthesis of diverse nitrogen-containing heterocycles.[2] Generally, triazole in a reversible ring−chain tautomerization equilibrium could give rhodium azavinyl carbene (Rh-AVC) in the presence of rhodium(II) catalyst.[3] Rh-AVC was equipped with highly electrophilic carbenoid carbon and highly nucleophilic α-imino nitrogen, thus particularly effective in transannulation with unsaturated compounds.[2c−i]

In 2009, Fokin and co-workers reported the first Rh(II)-catalyzed asymmetric cyclopropanation of stable and readily available *N*-sulfonyl-1,2,3-triazoles with monosubstituted alkenes (Scheme 1a).[4a] Later, they found triazole generated *in situ* reacted with an electron rich olefin, leading to the [2 + 3] transannulation product (Scheme 1b).[4b] A similar transformation was achieved by Anbarasan's group with ether-tethered ethylene utilized in 2014 (Scheme 1b).[4c] In continuation of our interest in the development of metal carbenoids,[5] herein we report a novel Rh-catalyzed functionalization of triazoles with alkenes, which enable the rapid access of diverse allyl dihydronaphthalene via formal allylation (Scheme 1c).

We initiated our investigation by conducting the reaction of dihydronaphthotriazole **1a** and α-methylstyrene **2a** under a commonly used catalyst system (Table 1, entries 1−5), among which $Rh_2(OPiv)_4$ exhibited superior reactivity by affording the desired product **3a** in 89% yield (entry 5, in bold). To our surprise, there was no cyclopropanation product detected. Reducing the ratio of **2a**/**1a** or changing the temperature would diminish the yield of **3a** (entries 6−8). In addition, exploration of several other solvents resulted in decreased yields (entries 9−11).

Scheme 1. Rh(II)-Catalyzed Reaction of Terminal Alkenes with 1,2,3-Triazoles



With the optimal reaction conditions in hand, we then examined the scope and functional group tolerance of this allylation reaction. As shown in Scheme 2, the reaction was applicable to various substituted α-methylstyrenes. For example, alkenes containing alkyl, halogen, ether, aryl, and even sulfoxide groups on benzene ring were competent in this reaction, producing formal allylation products **3a**−**o** in 53−90% yields. It is obvious that styrenes bearing donating groups (**3b**−**c**, **3j**−**k**, **3n**−**o**, 75−90%) generally performed better than

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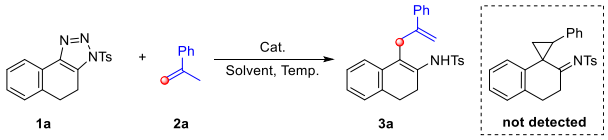
Table 1. Optimization of the Reaction Conditions[a]



entry	cat (1 mol %)	2a (eq)	sol	temp (°C)	3a[b] (%)
1	IPrAuCl	2.0	DCE	60	NR
2	$Pd(PhCN)_2Cl_2$	2.0	DCE	60	NR
3	CuI	2.0	DCE	60	NR
4	$AgNTf_2$	2.0	DCE	60	NR
5	**$Rh_2(OPiv)_4$**	**2.0**	**DCE**	**60**	**89**
6	$Rh_2(OPiv)_4$	1.0	DCE	60	42
7	$Rh_2(OPiv)_4$	2.0	DCE	40	37
8	$Rh_2(OPiv)_4$	2.0	DCE	80	51
9	$Rh_2(OPiv)_4$	2.0	CH_3CN	60	NR
10	$Rh_2(OPiv)_4$	2.0	toluene	60	31
11	$Rh_2(OPiv)_4$	2.0	DCM	60	59

[a]The reaction was performed under N_2 for 12 h; **1a** (0.1 mmol), 60 mg of 4 Å M.S. (molecular sieve) in 1 mL of solvent. [b]The yield of **3a** was determined by ^1H NMR spectroscopy with dimethyl terephthalate as the internal standard.

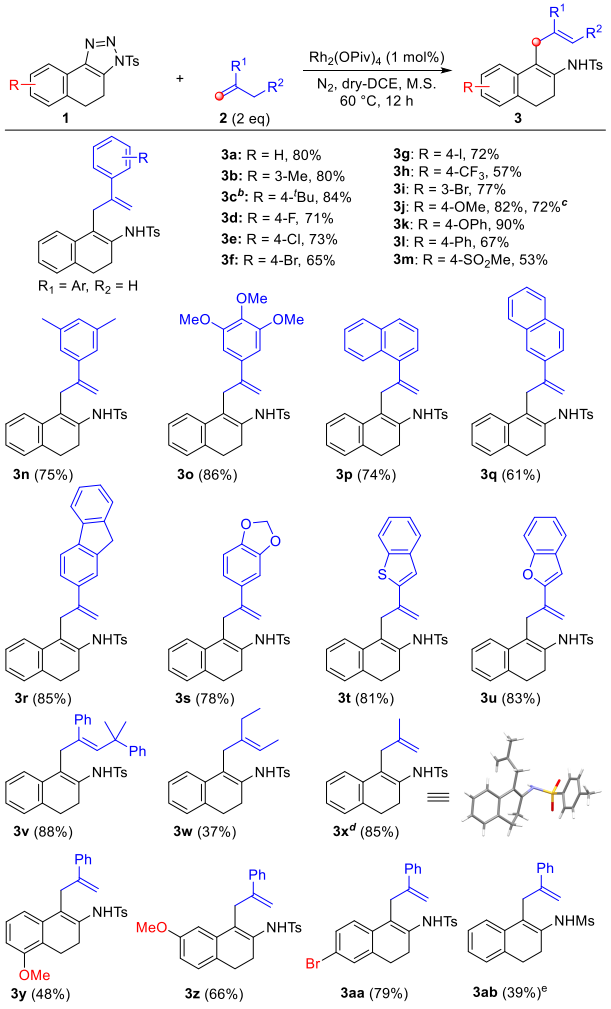
those bearing electron-withdrawing groups (**3d−i**, 65−77%). In addition, the position (**3f** and **3i**) and the number of substituents (**3n** and **3o**) had slight influence on the reaction yield. Phenyl and sulfoxide groups on the α-methylstyrene only gave the desired products **3l** and **3m** in moderate yields (67% and 53%) probably due to poor solubility. Notably, the reaction of *tert*-butyl-substituted alkene required higher temperature (**3c**). Besides, the reaction could be carried out at the 2 mmol scale and provided **3j** without a noticeable decrease of the yield (72%).

Other substituents on alkenes were also examined. Sterically hindered, naphthyl-substituted alkenes afforded the products **3p** and **3q** in 74% and 61% yields, respectively. Alkenes containing fluorenyl, acetal, and heteroaryl (such as benzothiophenyl and benzofuranyl) groups also worked well and furnished the corresponding allyl dihydronaphthalene (**3r−u**) in good yields (78−85%). Surprisingly, the reaction of alkene bearing bulky alkyl substituent at the β-position succeeded in providing the expected product **3v** in excellent yield of 88%. However, another alkylalkene 2-ethylbutene resulted in a messy situation and produced **3w** in only 37% yield, presumably due to the presence of β-C(sp^3)−H. It is worth mentioning that alkylalkene **3x**, similar to **3w**, was synthesized in good yield (85%) under neat condition, of which the structure was confirmed by X-ray diffraction analysis. When **1a** was treated with internal alkenes, unfortunately, none of them gave the desired products (see details in Supporting Information).

To further investigate the scope applicability of this reaction, triazoles with different substituents were next studied. Significantly, triazoles featuring electron-withdrawing groups (**3aa**) gave higher yields than those with electron-donating groups (**3y−z**), but slightly lower yields than that with an electron-neutral group (**3a**). The sulfonyl group of triazole could also be Ms and gave the desired product **3ab** in 39% yield.

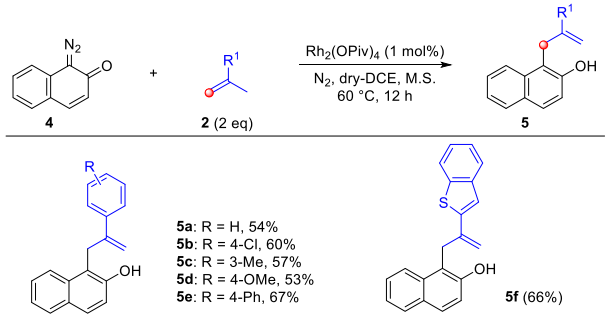
With the above encouraging results in hand, we moved on to explore the feasibility of this methodology in the systems involving diazo compounds (Scheme 3). Diazonaphthoquinone **4** was subjected to the reaction with α-methylstyrene derivatives **2**. To our delight, the reaction afforded formal allylation products as expected, rather than the traditional

Scheme 2. Substrate Scope of Triazoles and *gem*-Disubstituted Alkenes[a]



[a]Reaction conditions: N_2, 1 mol % $Rh_2(OPiv)_4$, **1** (0.2 mmol), **2** (0.4 mmol), 4 Å M.S. (120 mg), DCE (2 mL); isolated yield. [b]80 °C. [c]2 mmol of **1a**, 0.5 mol % $Rh_2(OPiv)_4$. [d]Neat reaction, 4 mL of isobutylene solution (2.0 mol/L in DCM). [e]*N*-Ms-protected triazole was used instead.

Scheme 3. Substrate Scope of Alkenes with Diazonaphthoquinone[a]



[a]Reaction conditions: N_2, 1 mol % of $Rh_2(OPiv)_4$, **4** (0.2 mmol), **2** (0.4 mmol), 4 Å M.S. (120 mg), DCE (2 mL), 12 h, isolated yield.

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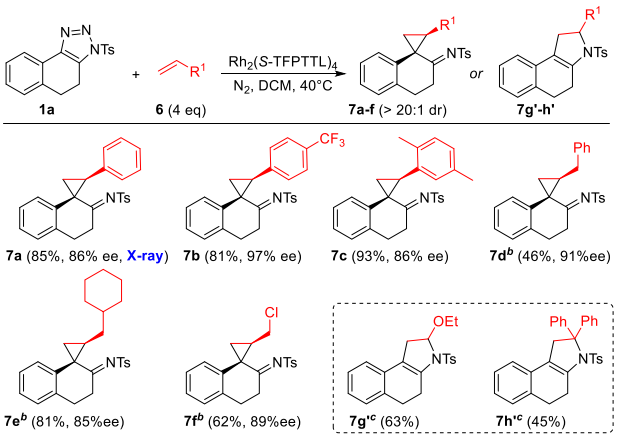
cyclopropanation products.[6] Various alkenes bearing electron-donating, electron-withdrawing, as well as heteroaryl groups were then tested under the standard conditions, giving products **5a**–**f** in moderate yields (53–67%). The relatively low yields are probably caused by the oxygen atom that exhibits a lower nucleophilic character than the nitrogen atom of the azavinyl carbene.[7] Other carbene precursors such as benzotriazole and diazoindene were also tested; however, they were not compatible with this allylation reaction (see details in Supporting Information).

In addition to α-methylstyrene derivatives, we also investigated the transannulation of naphthotriazole **1a** with styrene derivatives **6** in the presence of 1 mol % Rh_2(*S*-TFPTTL)$_4$ (Scheme 4). Traditional cyclopropanation took

Scheme 4. Transannulation of Naphthotriazoles with Monosubstituted Terminal Alkenes[a]

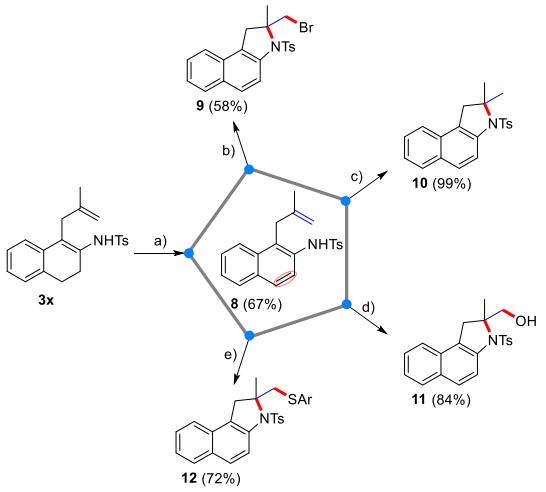


[a]Reaction conditions: N_2, **1a** (0.1 mmol), **6** (0.4 mmol), 1 mol % Rh_2(S$^-$TFPTTL)$_4$, 4 Å M.S. (100 mg), 1 mL of distilled DCM, 24 h; isolated yield. [b]60 °C. [c]2 days.

place in the reaction of alkyl- and aryl-substituted alkenes, giving cyclopropanes (**7a**–**f**) in moderate to high yields (46–93%) and good enantioselectivities (85–97% ee). When it came to ethyl vinyl ether as substrate, the introduction of an ether functionality caused the formation of dihydropyrrole **7g′** in moderate yield, which was similar to phenomenon found by Anbarasan and co-workers.[4c] Similarly, 1,1-diphenylethylene **6h**, unlike styrene **6a**, underwent further isomerization into dihydropyrrole **7h′** in 45% yield. These results indicated the selectivity of naphthotriazoles transformation could be easily tuned by substituents of terminal alkenes. The absolute configuration of cyclopropanes was confirmed by X-ray diffraction analysis.

Further transformation of the allyl dihydronaphthalene product **3x** was then investigated to demonstrate the potential synthetic utility of this reaction (Scheme 5). We treated **3x** with a variety of oxidants for aromatization, including TBHP, DDQ, MnO_2, and selectfluor. It turned out that only selectfluor succeeded in the oxidation of **3x**, furnishing naphthalene **8** in 67% yield. Naphthalene **8** can undergo a variety of 5-exocyclizations, delivering the corresponding functionalized indolines **9**–**12** in moderate to excellent yields. For example, bromoamination of **8** with *N*-bromosuccinimide (NBS) afforded 2-(bromomethyl)pyrroline **9** in 58% yield.[8] Treating **8** with boron trifluoride–diethyl ether gave rise to almost quantitative yield of cyclization product dihydropyrrole

Scheme 5. Further Transformation of 3x[a]

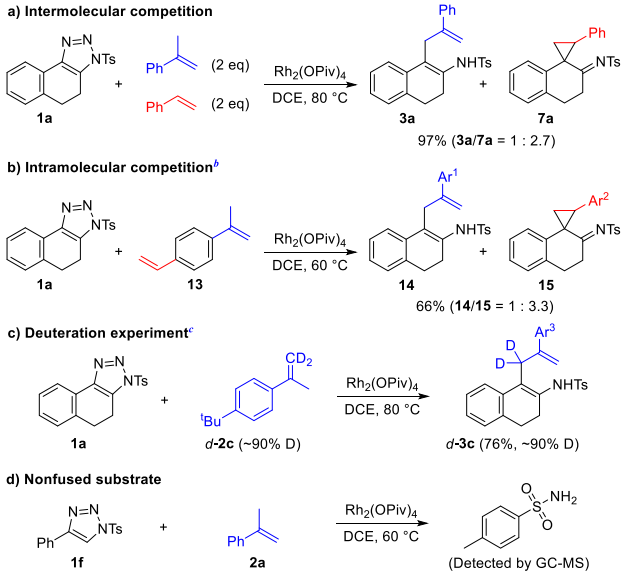


[a]Selectfluor, DCM, 60 °C. [b]NBS, toluene/DCM, 70 °C. [c]BF_3·Et_2O, DCM, 0 °C, rt. [d]*m*-CPBA, DCM, rt. [e]4-^{t}BuC_6H_4SH, NFSI, CuCl, B_2Pin_2, CH_3CN, 45 °C; Ar = 4-*tert*-butylphenyl.

10.[9] In addition, C–O and C–S bonds can also be constructed according to Li's[10] and Zhu's[11] work, giving the desired product **11** and **12** in 84% and 72% yield, respectively.

To clarify the mechanism, several control experiments were carried out. First, the reaction of **1a** with equivalent styrene and α-methylstyrene afforded an isomeric mixture of **3a** and **7a** in 97% total yield with a 1:2.7 ratio (Scheme 6a), clearly

Scheme 6. Control Experiments[a]



[a]Reaction condition: N_2, alkene (2 equiv), isolated yield. [b]Ar^1 = 4-vinylphenyl, Ar^2 = 4-isopropenylphenyl. [c]Ar^3 = 4-*tert*-butylphenyl.

indicating that cyclopropanation proceeded faster than allylation and suggesting the former course possesses higher reactivity. This result is also supported by another intramolecular competition reaction with the mixture products of **14** and **15** (1:3.3) in 66% total yield (Scheme 6b). When methylstyrene *d*-**2c** (90% D) with deuterated methylene was employed as substrate, the deuterium was introduced onto the methylene carbon atom of the product *d*-**3c** without

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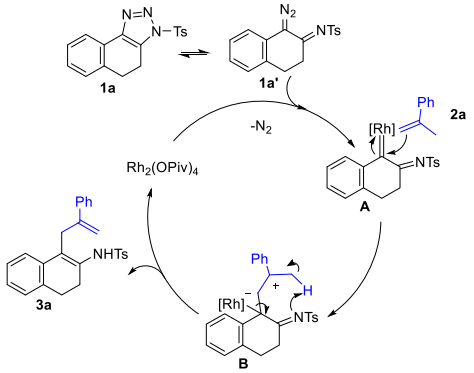
measurable scrambling of the isotope label (Scheme 6c). In addition, the reaction of acyclic triazole **1f** with α-methylstyrene was also performed but the substrate decomposed into $TsNH_2$[12] and no formal allylation product could be detected (Scheme 6d), which implied the importance of the cyclic effect of the triazole substrate (see details in the Supporting Information for more control experiments).

Based on the above control experiments, a plausible reaction mechanism of **1a** with **2a** is presented in Scheme 7. The

Scheme 7. Proposed Mechanism of the Formal Allylation



reaction is initiated by electrophilic attack of Rh(II) into the nucleophilic diazo compound **1a′**, which exists in a closed/opened form equilibrium with the triazole **1a**.[13] Subsequently, nitrogen eliminates from **1a′** and rhodium carbenoid intermediate **A** is generated. After nucleophilic attack of α-methylstyrene **2a** onto the electrophilic rhodium carbenoid carbon of **A**, the formed charged transition state **B** undergoes an intramolecular proton transfer to furnish the desired product **3a** and regenerates the dirhodium catalyst. The *cis*-oriented C═N geometry and the basic nitrogen atom might facilitate the proton elimination of the $C(sp^3)$—H.

In summary, we have developed a formal allylation of alkenes with rhodium azavinyl carbenes generated *in situ* from dihydronaphthotriazoles. This unique process also can be compatible with the diazo compounds. An intramolecular proton transfer was proposed to account for the unusual allylation reaction. When monosubstituted alkenes are used, cyclopropanation is dominated and good enantioselectivities have been achieved.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c04251.

Experimental details and characterization data of all new compounds; structures, spectra, crystallographic data, NMR spectra, and HPLC data (PDF)

Accession Codes

CCDC 1970500 and 2047547 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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